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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,098	12/05/2003	Klaus Bosslet	DORRIE-0007	7295
23599	7590	09/26/2006	EXAMINER	
MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201			PESELEV, ELLI	
			ART UNIT	PAPER NUMBER
			1623	

DATE MAILED: 09/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/728,098

Applicant(s)

BOSSLET ET AL.

Examiner

Elli Peselev

Art Unit

1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 August 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-10, 12 and 23-32 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10, 12 and 23-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

Claims 1-10, 12 and 23-32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A conclusion of lack of enablement means that, based on the evidence regarding each of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation.

(A) Breadth of the Claims.

The claims encompass an immense number of species. Note that the number of variables in claim 1 exceeds 100.

(B) The predictability or lack thereof in the art.

Relative minor changes in epothilone compounds can convert a drug that is active cytotoxic agent to a drug that is inactive. Note, for example, that Nicolaou et al (U.S. Patent No. 6,441,186) disclose in Example 5, column 46 that while oxazole analogs had cytotoxic activity comparable to thiazole analogs, the 4,4-ethano-epothilones proved inactive. Nicolau et al further state that "These results underscore the importance of conformational precision in these compounds for biological activity".

(C) The presence or absence of working examples.

No working examples showing an activity for any of the claimed compounds have been presented.

(D) The quantity of experimentation needed.

Because there is no way to predict a priori which compounds will be active from the specification or chemical structures alone, an extraordinary amount of trial and error experimentation is required to identify the active compounds.

Applicant's arguments filed August 7, 2006 have been fully considered but they are not persuasive.

Applicant contends that anti-proliferative activity of epothilone compounds is known in the art. While epothilone compounds are known cytotoxic, it cannot be predicted which claimed analogs will have a comparable activity since even minor structural changes in a compound can result in a compound with no cytotoxic activity as disclosed by Nicolaou et al (U.S. Patent No. 6,441,186) in Example 5. Also, the prior art is unaware of successful treatments of proliferative diseases, including inflammatory diseases, neurodegenerative diseases, angiogenesis-associated diseases, multiple sclerosis, Alzheimer's disease and rheumatoid arthritis as encompassed by claim 25 with chemically analogous compounds. The prior art patents cited by applicant do not provide any evidence of any other activity of epothilones, except the anti-tumor activity. Note that drug discovery is one of the most labor intensive and expensive types of inventions; it can cost over \$500 million to bring a single new drug to market. The specification fails to provide any evidence of any activity for the claimed compounds. Since the claimed compounds have significant structural differences from the prior art compounds, it cannot be predicted if the claimed compounds will have activity which is comparable to the activity of the prior art compounds.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A preamble in claim 9 states that "conjugate compound according to claim 1, whereby the portion of the compound represented by formula (I) ". Said terminology renders claim 9 indefinite since claim 1 only encompasses the compounds of formula (I). It is unclear which portion is referred to. Note, that in claim 1, the compounds of formula (I) include the linker-recognition unit of formula III. Therefore, there is no antecedent basis in claim 1 for the compounds of claim 9, since compounds of claim 9 fail to include a linker-recognition unit.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elli Peselev whose telephone number is (571) 272-0659. The examiner can normally be reached on 8.00-4.30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Jiang can be reached on (571) 272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elli Peselev

  
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